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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/900,699 | 07/06/2001 | Thomas J. Brennan | R-173 | 3947 |

7590 11/05/2002

Deltagen, Inc.
740 Bay Road
Redwood City, CA 94063

EXAMINER

QIAN, CELINE X

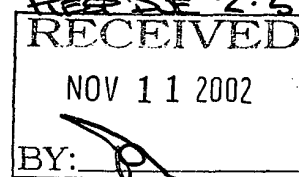
ART UNIT

PAPER NUMBER

1636

DATE MAILED: 11/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.



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Office Action Summary



Application No.

09/900,699

Applicant(s)

BRENNAN, THOMAS J.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 11-16 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 17-19 is/are rejected.
- 7) ☒ Claim(s) 2 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5, 13. 6) ☐ Other: _____

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DETAILED ACTION

Claims 1-20 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I-VIII are related and a search for all 8 groups can be made without burden.

This is not found persuasive. The inventions of Groups I-VIII are patentably distinct for reasons set forth of the record mailed on 9/6/02. A search of the subject matter of one invention would not be co-extensive with a search of the other inventions, and therefore the additional search effort involved in searching all 8 inventions in a single application would be burdensome. Each invention is capable of supporting a separate patent.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 11-16 and 20 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-10 and 17-19 are currently under examination on merits.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim is drawn to a construct comprising a screening marker.

Since it's unclear how it is different from the "selection marker," claim 2 fails to limit the subject matter of claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a homozygous knockout mouse comprising a homozygous disruption in the DEZ receptor gene, wherein no functional DEZ receptor is produced, and exhibiting phenotypic features such as decreased agility or coordination as compared to wild type mice, a method of producing such a transgenic mouse, and a cell isolated from the knockout mouse, does not reasonably provide enablement for other transgenic and/or knockout animal comprising any disruption in any DEZ receptor homolog gene. Further, the specification is not enabling for a knockout mouse comprising any disruption in any DEZ receptor homolog gene and for any cell comprising any disruption in a DEZ receptor homolog gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior

art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the Invention:

Claims 5-10, 17-19 are drawn to a cell comprising a disruption in a DEZ receptor homolog gene, a non-human transgenic animal comprising a disruption in a DEZ receptor homolog gene, a cell from that transgenic animal, and a method of producing the mouse with any disruption in said gene. Thus, the nature of the invention is directed to transgenic animals and methods of producing the transgenic animals.

Breadth of Claims:

In the instant case, claims 1-10, 17-19 encompass any transgenic animal containing any disrupted allele for the gene that encodes any DEZ receptor homolog. Further, the claims encompass any knockout mouse comprising any disruption in DEZ receptor homolog gene and exhibiting the phenotypes of decreased agility or coordination as compared to wild type mice. Further, the claims encompass any cell comprising any disruption in a DEZ receptor homolog gene and encompass all cells capable of undergoing homologous recombination (specification page 7, lines 3-5). The disruption, as disclosed in the specification (page 6, line 25-31) includes any insertion, deletion or substitution in any portion of the gene (introns, exons, regulatory regions). The claims, therefore, encompass all such disruptions and also cover all animals that contain DEZ receptor homolog gene disruption (page 7, lines 6-9).

The specification does not provide an enabling disclosure for the full scope of transgenic animals of the type claimed. The only embodiment enabled by the specification within the scope of claims 1-10, 17-19 is for a homozygous knockout mouse comprising a disruption in the DEZ receptor gene that results in loss of function of the DEZ receptor gene and exhibiting phenotypic features of decreased agility or coordination as compared to wild type mice, a method of producing such a transgenic mouse. Thus the breadth of claims is very broad and encompasses any transgenic animal and a knockout mouse with any disruption in any DEZ receptor gene and includes any and all mutant forms, substitutions, deletions, or insertions in any DEZ receptor gene (specification, page 7, lines 15-23).

Amount of guidance in the specification and Working Examples:

The specification discloses the use of a specific DEZ receptor gene as set forth in SEQ ID NO:1 in producing a homozygous transgenic knockout mouse, wherein the knockout mouse exhibits phenotypic changes that include decreased agility or coordination as compared to wild type mice.

The specification and the working examples provide sufficient guidance to practice the invention with only a homozygous, knockout mouse containing two disrupted alleles for the gene that encodes a murine DEZ receptor gene of SEQ ID NO:1 wherein the disruption results in loss of function of the DEZ receptor gene. The specification does not teach how to make and use the invention with other species of transgenic or knockout animals nor with any knockout mouse with any form of disruption in the gene encoding DEZ receptor, as claimed in the claims 1-15, 17-19. Further, the specification does not teach how to make and use any cell comprising any

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type of disruption in a DEZ receptor gene as claimed. The scope of claims 1-10, 17-19 thus surpasses that enabled by the specification.

State of the Art, Predictability or Unpredictability of the art, Amount of experimentation necessary and Skill level of the artisan:

Although the skill of an artisan in this subject area is considered to be very high, it would require undue experimentation on the part of an artisan to make and use the claims as specified and use the invention with any and all transgenic animals as claimed. The specification and the working examples provide sufficient guidance to practice the invention with only a homozygous, knockout mouse containing two inactivated alleles for the gene that encodes a murine DEZ receptor wherein the knockout mice exhibit decreased agility or coordination. However, neither the specification nor the working examples provide enough guidance on how to practice the invention with any and all transgenic animals and/or transgenic mice carrying any and all transgene(s) of the types recited in the claims.

When considering the predictability of this invention, one has to remember that many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studied and the effect of allelic variation and the interaction between the allelic variants (pg.1425, paragraph 1 in Sigmund, C.D. 2000. Arterioscler Thromb Vasc Biol.20:1425-1429). The specification discloses the phenotype of a homozygous DEZ receptor gene knockout mouse comprising a disruption in the DEZ receptor gene comprising the sequence set forth in SEQ ID NO:1 and fails to disclose the phenotype of other knockout animals with a disruption in DEZ receptor gene. Given the state of art, the phenotype of a transgenic or knockout animal is unpredictable. Thus, the specification, in the instant case, is not enabling for

transgenic and/or knock out animals, including mice, that exhibit no phenotype or that exhibit transgene-dependent phenotypes other than that disclosed in the instant specification.

Further, transgene expression and the physiological consequences of transgene products are not always accurately predicted in transgenic mouse studies (pg.62, paragraph1, lines 7-9 in Wall, R.J. 1996. Theriogenology 45:57-68). Thus, the invention while being enabled for a homozygous knockout mouse containing two disrupted alleles for the gene comprising the sequence set forth in SEQ ID NO:1 and encodes a DEZ receptor, does not extend the predictability of the invention to other animal systems.

The particular genetic elements required for expression varies from species to species. Our lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior (Wall, 1996). Therefore, the phenotype of knockout animals is not predictable. For example, Jacks et al. (1992) describe Rb knockout mice that do not display retinoblastoma; rather they exhibit the unexpected phenotype of pituitary tumors. The pituitary tumors arise from cells lacking a wild-type Rb allele. Thus, tumors were found to arise not in retinas, as in humans, but in the pituitary gland (page 299, Discussion, paragraphs 1 and 3). Therefore, in the absence of specific guidance and working examples, the production of transgenic animals with the scope as claimed is unpredictable. In such a situation, one skilled in the art would not know how to make and use the full scope of the invention as claimed, without undue experimentation.

The specification fails to provide an enabling disclosure for the preparation of other species of knockout animals besides mice having a disruption in the DEZ receptor gene because the guidance offered in the specification is limited to the preparation of mice harboring such

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mutations and no teachings or guidance are offered in regard to how one would have prepared any other type of animal having the recited gene disruption. Since homologous recombination is required for gene targeting methods such as employed in the instant invention, embryonic stem (ES) cell technology must be available to carry out the method. At present, there is no evidence to support that a transgenic knockout mouse can be generated from other types of cell comprising a disruption in a specific gene. The only species in which such technology was known was the mouse and the artisan did not accept that it was possible to have prepared ES cells in other species (see e.g. Bradley et al., paragraph bridging pages 537-538). Campbell and Wilmut, 1997 acknowledge reports of ES-like cell lines in a number of species, but emphasize that as yet there are no reports of any cell lines which contribute to the germ line in any species other than the mouse (p. 65). Likewise, Mullins et al. (1996) teach that "[a]lthough to date chimeric animals have been generated from several species including the pig, in no species other than the mouse has germline transmission of an ES cell been successfully demonstrated. This remains a major goal for the future and may well require the use of novel strategies which depart widely from the traditional methods used in the mouse" (p. S38, column 1, paragraph 1. Thus, knockout animals cannot be prepared for any species other than the mouse. Since ES cell technology was required to produce the claimed animals and practice the claimed methods of using such animals, in the absence of such technology available in other species, one skilled in the art would have been required to exercise undue experimentation to produce the full scope of claimed animals and to practice the claimed methods in species other than mice.

In view of the limited guidance in the specification, and limited working examples directed to transgenic, knockout mice with a specific knockout gene and exhibiting a specific

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phenotype, and the unpredictability of the art, one skilled in the art would be required to engage in undue experimentation, in order to make and use the invention in its full scope as claimed. Thus, the enabled scope of the claims is limited to a homozygous knockout mouse comprising an inactivating deletion in the DEZ receptor gene as set forth in SEQ ID NO:1 and exhibiting phenotypic features of decreased agility or coordination as compared to wild type mice, and a method of producing such a transgenic mouse.

Claims 1-10 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants are referred to the guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, No. 4, pp. 1099-1111 (also available at www.uspto.gov).

The specification does not provide or point to a written description of the genus of DEZ receptor genes recited in the claims. Claim 17 is directed to a transgenic and/or knockout mouse containing DEZ receptor or homolog gene disruption. However, the specification only describes a single species of a DEZ receptor gene; the murine gene of SEQ ID No:1. The specification fails to teach other "homologs" of SEQ ID NO:1 from other species of animals besides mice, or a "homolog" that has the same function as murine DEZ receptor. In analyzing whether a written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the claims encompass the whole genus of 'DEZ receptor or homolog genes' and

include any and all transgenic animals that contain any altered allele for the gene that encodes a DEZ receptor or a homology thereof. Thus for the claims to meet the written description requirement, other representative species of "DEZ receptor homolog genes", should be described by their complete structure or by other relevant identifying characteristics, in the specification.

Next, then, it is determined if a representative number of species have been sufficiently described by other relevant identifying characteristics. In the instant case, no identifying characteristics are provided for the genus of DEZ receptor homolog genes recited in the claims. Thus the limited information in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed genus of DEZ receptor homolog genes. Thus, it is concluded that the written description requirement is not satisfied for the claimed genus of "DEZ receptor or homolog genes".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-4 and 10, it is unclear how the target construct is arranged. In other words, is the first polynucleotide adjacent to the second polynucleotide or is there a selectable marker gene in between? Where is the screening marker located in the construct? In addition, it is also unclear whether the first and second polynucleotide is a contiguous sequence of the target

gene or just portions of the target gene. The arrangement of the elements is essential to the operability of the invention.

Regarding claims 1-4, the terms "selectable marker," "selection marker" or "screening marker" render the claim indefinite because it is unclear how a marker protein can be inserted in a vector construct. Use of term such as "selectable marker gene" is suggested.

Regarding claim 2, the term "screening marker" renders the claim indefinite because it is unclear what term encompasses. In other words, it is unclear how a "screening marker" differs from the "selection marker" recited in claim 1.

Regarding claim 9, the word "derived" renders the claim indefinite because the nature and number of derivative processes is unknown. Use of the term "isolated" is suggested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mansour et al (1988, Nature, vol. 336, No. 24, 348-352), in view of Methner et al (1997, BBRC, vol 233, No.2, pages 336-342. IDS) and Murphy et al (1998, Current Opinion in Drug Discovery and Development, vol. 1, No. 2, pages 192-199).

The claims are drawn to a DEZ receptor gene-targeting construct and a method of making said construct. The claims are further drawn to a cell and a transgenic animal comprising a

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disruption in a DEZ receptor, and a method of producing a transgenic mouse comprising a disruption in a DEZ receptor gene by homologous recombination using the target construct.

Mansour et al. teach a strategy for targeted disruption of the *hprt* gene and proto-oncogene *int-2* in mouse embryonic stem cells and subsequent generation of knockout mice. Their teaching addresses the previous technical difficulty of obtaining embryonic stem cell carrying non-selectable, targeted gene mutation at loci of interest, and therefore provides a model which can be used to produce homozygous mutation of any gene, regardless of its function, if a cloned fragment of the gene is available (see page 348, second paragraph, line 1-3, third paragraph, line 1-5, and page 352, fourth paragraph, line 1-3). Mansour et al. further teach the generation of two targeting constructs, pRV9.1/TK and pINT-2-N/TK, each contains two sequences from an *hprt* gene and an *int-2* gene respectively, and a neo selection marker gene in between the two sequences (see page 350, figure 3). However, Mansour et al. do not teach how to make a DEZ receptor target construct and knockout mouse.

Methner et al. teach the cloning and characterization of a novel G protein coupled receptor (GPCR), DEZ receptor, from a cell line and a cDNA library of adult mouse brain. Methner et al. further provide the nucleic acid sequence encoding DEZ receptor (see page 337, Figure 1).

Murphy et al. teach that GPCRs are the major structures through which physiological signals involving cellular and organism homeostasis are transduced across the cell membrane, and represent the largest single group of drug targets (see page 192, 1st col., 1st paragraph). Murphy et al. also teach that the physiological and pathophysiological function must be studied before the successful development of therapeutic compound (see page 192, 1st col., 2nd

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paragraph). Murphy et al. further teach that gene knockout studies in mice have provided strong support for targeting specific GPCRs for therapeutic development (see page 192, 2nd col., 3rd-4th paragraph).

It would have been obvious to one of ordinary skill in the art at the time of filing to make a DEZ knockout construct and a transgenic knockout mouse because of the combined teaching of Mansour et al., Methner et al. and Murphy et al. The ordinary artisan would have been motivated to do so to study the physiological and pathophysiological function of DEZ receptor in order to make it a therapeutic target for developing new drugs, as taught by Murphy et al. One of ordinary skill in the art would have reasonable expectation of success to make a DEZ receptor knockout mouse because of the teaching of Mansour et al., who teach a method of generating a homozygous mutation of any gene in mouse, and Methner et al., who provide the sequence information required for generating a DEZ knockout mouse. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

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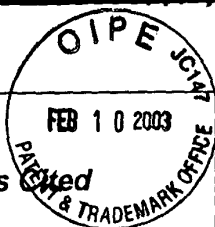
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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
November 4, 2002

Anne-Marie Zalk
ANNE-MARIE BAKER
PATENT EXAMINER

Notice of References Cited



Application/Control No.

09/900,699

Examiner

Celine X Qian

Applicant(s)/Patent Under
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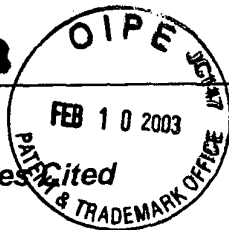
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| | W | Bradley et al. Modifying the Mouse: Design and Desire. May 1992. Biotechnology. Vol. 10, pp. 534-539. |
| | X | Mullins and Mullins. Perspective Series: Molecular Medicine in Genetically Engineered Animals. April 1, 1996. Clinical Investigation. Vol.97, No.7, pp. 1557-1560. |

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

**Notice of References Cited**

Application/Control No.

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Applicant(s)/Patent Under
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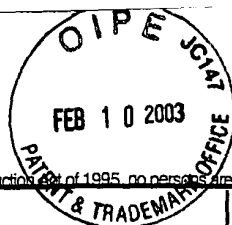
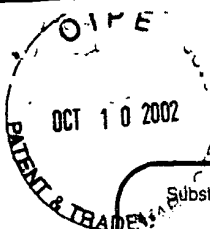
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| | X | Murphy et al. From DNA to Drugs: the orphan G-protein Coupled Receptors. 1998. Current Opinion in Drug Discovery and Development. Vol. 1, No. 2, pp.192-199. | | | | |

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
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#13

PTO/SB/08A (10-01)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
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(use as many sheets as necessary)

Sheet 1 of 2

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| Application Number | 09/900,699 |
| Filing Date | July 6, 2001 |
| First Named Inventor | Thomas J. Brennan |
| Art Unit | 1636 |
| Examiner Name | Qian, Celine X |
| Attorney Docket Number | R-173 |

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U.S. PATENT DOCUMENTS

| Examiner | Cite No. ¹ | Document Number | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|----------|-----------------------|--|--------------------------------|--|---|
| | | Number Kind Code ² (if known) | | | |
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| | AB | US- | | | |
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| | AE | US- | | | |
| | AF | US- | | | |
| | AG | US- | | | |

FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | | | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁵ |
|-----------------------|--------------------------|---------------------------|---------------------|-----------------------------------|--------------------------------|---|--|----------------|
| | | Country Code ³ | Number ⁴ | Kind Code ⁶ (if known) | | | | |
| CA | AH | PCT | WO 97/47316 | A1 | 12/18/97 | Millennium Pharm. | | |
| r | AI | PCT | WO 98/53071 | A1 | 11/26/98 | Biogen, Inc. | | |
| | AJ | | | | | | | |
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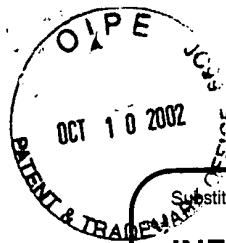
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| Examiner Signature | | Date Considered | 10/24/02 |
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(use as many sheets as necessary)

Sheet 2 of 2

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|------------------------|-------------------|
| Application Number | 09/900,699 |
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OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

| Examiner Initials * | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|------------------------|--------------------------|---|----------------|
| WQ | AQ | MADHAVI J. RANE, et al. "Activation of Mitogen-activated Protein Kinases by Formyl Peptide Receptors is Regulated by the Cytoplasmic Tail" <i>The Journal of Biological Chemistry</i> , Vol. 273(33), Aug. 14, 1998, pp. 20916-20923 | |
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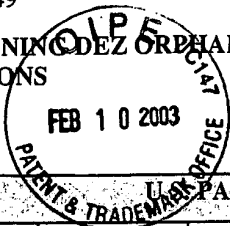
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DISCLOSURE CITATION
PTO-1449

TRANSGENIC MICE CONTAINING ORPHAN
RECEPTOR GENE DISRUPTIONS

Date: October 24, 2001



Atty Docket:
R-173

Serial No.:
09/900,699

Applicant:
BRENNAN

Filing Date:
July 6, 2001

Group Art Unit:
Unassigned

U.S. PATENT DOCUMENTS

| EXAMINER'S INITIALS | PATENT NO. | DATE | NAME | CLASS | SUBCLASS | FILING DATE |
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| EXAMINER'S INITIALS | PATENT NO. | DATE | COUNTRY | CLASS | SUBCLASS | Translation | |
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OTHER DOCUMENTS: (Including Author, Title, Date, Pertinent Pages, Etc.)

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| cd | Methner, A. et al., <u>Biochem and Biophys. Res. Commun.</u> , 233(2):336-342 (1997), "A Novel G Protein-Coupled Receptor with Homology to Neuropeptide and Chemoattractant Receptors Expressed during Bone Development" |
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| EXAMINER <u>[Signature]</u> | DATE CONSIDERED <u>10/24/02</u> |
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